Lawyer's Work Product

F - Staff General Research

M E M O R A N D U M

FROM: CHARLES R. WALL

DATE: SEPTEMBER 21, 1984

RE: RESEARCH CONDUCTED AT PHILIP MORRIS

During the past months there has been considerable discussion regarding the correct way to characterize the research that has been done at Philip Morris. The discussion has concerned itself with whether the research relates to smoking and health. In the process of preparing for the briefings of Drs. Osdene and Wakeham, we have reviewed a number of research documents and this memorandum sets forth some of the comments in those documents which I believe will be helpful in appropriately characterizing some of the research done at Philip Morris.

In 1956 Dr. DuPuis wrote a memorandum to McComas, Cullman, Weissman and Hatcher discussing proposed irritation work to be done by Dr. Paul Kotin at USC. The research involved the study of the irritant effects of smoke and whether a ventilated cigarette might be advantageous to the company in "an aggressive counter-attack on the health charges which have been made against cigarette smoking." The advantages which DuPuis saw in a better ventilated cigarette were an increase in the oxygen content of the smoke and subjectively decreased irritation by the smoke. DuPuis states that the decreased irritation is desirable not only from the subjective viewpoint but also as a partial elimination of a potential cancer hazard. DuPuis hypothesizes that irritation of lung cilia can decrease or eliminate the ability of the cilia to remove foreign substances such as smoke solids from the lung. Extreme irritation might also lead to damage to lung cells, with an increased chance of successful attack by foreign substances in the lung.

We should remember that this sort of discussion is taking place in July of 1956.

In a 1961 report to the products committee, Wakeham states that the accomplishments for 1960 in the "defensive" developments area were: cataloging over 700 tobacco and smoke constituents; developing a routine method for identifying polynuclear hydrocarbons and polyphenols and preliminary development

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of an objective test for smoke irritants. I suggest that the foregoing are related to research in the smoking and health area.

In a report dated March 27, 1963, and distributed to Hugh Cullman, et al., Dr. Wakeham makes the point that if a dose-response relationship exists between "cigarette smoke condensate" and lung cancer in humans, then the predictions of future lung cancer cases associated with smoking will be erroneous because they are based on statistical evidence from smokers smoking cigarettes with much higher concentrations of smoke condensate (TPM). Wakeham discusses some retrospective and prospective studies on smoking and lung cancer and states that these studies were done on smokers who do not have access to the "presently available low tar non- filter or filter cigarettes." This document shows a familiarity on the part of Wakeham with retrospective and prospective epidemiological studies together with an appreciation of the arguments regarding the relationship between smoke condensate and lung cancer.

Soon after the 1964 Surgeon General's Report was made public, Wakeham sent a memorandum to Hugh Cullman, Adkins, Britton Lincoln and Macon entitled "Smoking and Health Significance of the Report of the Surgeon General's Committee to Philip Morris Incorporated." This is probably one of the first responses given by a research person to top management in the report. Cullman was given ten copies of the memo presumably to be distributed among top management. Although Wakeham refers to the health impact as a basis for competition in the industry in the future and concludes that the individual companies must do their own research if they expect to develop proprietary positions for the health competition, the thrust of the memorandum is to propose work that should be done in light of the health claims against the product. Wakeham advocates the prompt and effective establishment of suitable biologically approved specifications for all new smoking products. This is to be done in an attempt to be in a position to exploit and influence any uniform and reliable testing procedures which the government might impose upon the industry in the health area.

In the above memorandum Wakeham says that as a direct result of the Surgeon General's Report Philip Morris research and development people intend to promptly review the literature to see what bioassay techniques can be used both at the Center and elsewhere to define optimum criteria for the use in physiological studies. The criteria will include a quick test for chemical carcinogenicity and the best measure of pulmonary cleansing effectiveness (ciliastasis and mucous flow). In addition, the R&D people will try to develop a filter cigarette marketly better

than any anticipated from the competition. The filter will permit the satisfactory functioning of pulmonary cleansing mechanisms and provide a flavor sufficient to attract a reasonable market. The Center will also emphasize a program studying the gas phase absorption and tar fraction carcinogenicity and scientists will be assigned to expand the Center's knowledge of developments in epidemiology and cancer studies (clinical as well as animal). Wakeham also urges the association with a first-class medical school. Wakeham concludes that the "industry must come forward with evidence to show that its products, present and prospective, are not harmful. The industry should abandon its past reticence with respect to medical research. Indeed, failure to do such research could give rise to negligence charges."

The document I have just referred to is evidence of the interest on the part of senior researchers in identifying and pursuing research relating to the smoking and health issue. Wakeham is advocating greater familiarity with epidemiological and biological studies, liaison with a first-class medical school, development of a better filter cigarette to better regulate TPM and to permit satisfactory function of the pulmonary mechanisms and a complete review of bioassay techniques in order to provide criteria for use in physiological studies. The documents do not reveal whether all of Wakeham's recommendations were adopted, although we do know that Philip Morris was working with FDRL and Hazleton Labs while continuing to study the constituents of cigarette smoke and whole smoke condensate in its own laboratories.

In the Fall of 1968, Wakeham, with Osdene's assistance, wrote a memorandum to Goldsmith arguing for biological testing and research in-house. Wakeham argues in a November 1968 memo to Goldsmith that most of Philip Morris's products are directly related to the health field and that Philip Morris will have to deal with an increasing concern for the health aspects of its products. Therefore, Wakeham concludes, Philip Morris needs increased capabilities to investigate the health implications of tobacco. Wakeham argues that Philip Morris needs to obtain its own facts and data with regard to biological systems in order to avoid being surprised by information from outside sources and in order to interpret and understand the results of other biological studies. In other words, Wakeham is making the point that it will be difficult to criticize or assess the reliability of studies unless Philip Morris has done them itself. Wakeham also hints of his concern that the government will engage in comparative brand biological testing and that biological activity will be established as a criteria by which the consumer acceptability of a brand will be measured. In order to be accomplished and

confident in understanding biological systems, Philip Morris, Wakeham argues, must have a facility of its own in which to "develop, test, and subject our own products and other brands to biological studies so that we may have knowledge and confidence in this field."

Basically, the arguments for in-house work on biological systems is based on: (1) the need to avoid being surprised by information from outside sources, (2) the need to be able to criticize and assess the validity of the work of outside sources, (3) the need to establish the toxicological safety of the various additives or ingredients in Philip Morris products, and (4) the need to test the biological activity of competitive brands. All of these, in part, "because of the greater emphasis on the smoking and health controversy . . . ."

In July of 1969 Wakeham wrote Goldsmith to again suggest the need for biological research in testing by Philip Morris for two reasons: (1) because of greater emphasis on the smoking and health controversy and (2) because of Philip Morris's involvement in health-sensitive non-tobacco product lines. Apparently, the July memorandum was a response to Goldsmith's request for a specific proposal for a biological research program based on the projected needs of the company for the next five years. The areas of recommended activity were: (1) inhalation studies, (2) test for carcinogenic activity, (3) evaluation of new bioassay tests, (4) radiochemical experimentation, (5) experimental animal behavior in relation to smoking patterns and (6) screening and toxicologic testing of new materials. Wakeham recommends that the above projects be carried out through an in-house facility. A quicker way, however, to do such testing would be acquire Woodard Research Corporation and to operate it as an in-house biological laboratory. Another alternative, Wakeham suggests, would be to use an outside biological testing laboratory which would cost a great deal more. It appears that a major reason for the increased interest in biological testing was the Tobacco Working Group's activities in the same area. The TWG was about to undertake: (1) skin painting, (2) intubation and intratracheal installation of condensate in experimental animals, (3) a bioassay with respect to cytotoxicity and effect on cell function and (4) the study of particulate materials in respiratory carcinogenesis. Another development was the initiation of smoke inhalation studies by CTR. (Reynolds and Philip Morris played a prominent role in the development of suitable smoking machines and inhalation chambers for use by CTR.)

Wakeham proposes inhalation studies in order to determine in different animal species the acute and chronic effects of

smoke from various tobaccos. Wakeham also proposes tests for carcinogenic activity, such as the mouse skin painting, which will enable Philip Morris to compare different cigarettes and different process modifications. Also, Wakeham proposes that PM evaluate new bioassay tests to determine how useful they are for short-term testing, mainly in terms of lung clearance. Wakeham also proposes radiochemical testing in order to study the disposition of smoke components in animals by using radioactive materials. The research would include the study of the deposition and clearance from the respiratory tree of smoke and its components. The experimental animal behavior research would study the "smoking behavior" of animals and its relation to environmental stress and genetic background. Wakeham reaffirms the recommendation of R&D that Woodard be purchased.

In August 1969 Wakeham sent another memo to Goldsmith updating his July 1969 memo and continuing to argue for an in-house biological research program.

Wakeham continues the argument in a September 9, 1969 memo to Cliff Goldsmith reporting on the skin painting data from the Harrogate Laboratories. The Harrogate data reported that cigarette smoke condensate painted on the backs of mice over a two-year period produced tumors in numbers proportionate to the amount of condensate applied. Wakeham notes that while the mouse skin painting carcinogenicity test has many short-comings, it is still widely accepted as the critical test for the biological activity of cigarette smoke. Wakeham notes that the TWG is also using the test as a primary assay of smoke and therefore, Wakeham argues, "Philip Morris should start testing its products now because it will be two years before it knows the answers."

In a memo dated September 16, 1969, from Millhiser to Weissman, Millhiser transmits Wakeham's proposal for an in-house biological research effort and strongly endorses it. Millhiser states "I strongly endorse the program and feel that further delay of its implementation would present undue risks to the corporation." Weissman passes Millhiser's memo on to Joe Cullman and states that he also strongly endorses the program. In what appears to be Weissman's handwriting notes state that Weissman recommends approval of the development of an aggressive in-house biological research and testing facility to fulfill Philip Morris's technical responsibilities and to acquire an on-going biological facility - up to $2 million.

In a memo dated October 7, 1969, from Joe Cullman to Millhiser, Cullman says that he still favors using CTR to sponser the biological activity research. He states that for legal,

philosophical and practical reasons a PM biological research program does not seem to have many advantages. Cullman states, however, that he is willing to keep the matter under active consideration and to review it at least quarterly.

In response to Joe Cullman's memo, Millhiser, on November 6, 1969, sent a memo to George Weissman saying that they should discuss the legal, philosophical and practical problems of Philip Morris mounting a biological research program and asked that Weissman set up a meeting to discuss those topics. A copy of the memorandum is sent to Goldsmith and Paul Smith.

On October 6, 1971, in a memorandum to the managers of R&D regarding the five-year strategic plan (1972-1976), Eichorn states that the company must be in a position to counteract outside anti-smoking efforts with strong definitive research programs. As a result, one of the major program objectives would be developing information demonstrating the benefits of cigarette smoking and defensive biological programs.

In a memo dated March 20, 1974, from Osdene to Seligman, with a copy to Charles, Osdene lists Philip Morris work being done at Inbifo (inhalation studies) and Bio-Research Consultants, Inc. (mouse skin painting) as part of the biological work regarding smoking and health being done on a world-wide basis.

There is an undated lengthy report found in Wakeham's files relating to the activities of the R&D center in the biological research areas. The form of it appears to be a presentation of information relating to the biological activity of specific tobacco blends. In addition, there is a review of the various long-term and short-term bioassays conducted by various organizations such as the National Cancer Institute, the VDC, Tobacco Research Council in England, CTR, University of Kentucky, Philip Morris, P. Lorillard, R. J. Reynolds, etc. Also with the document are reports on respiratory ailments as reported in epidemiological studies on black lung, nickel workers, uranium miners, asbestos workers in Ireland, and the effects of cigarette smoke on induction of B(a)P hydroxylase in rats. The title of the work is "Smoke Chemistry and the Bioassay".

In April of 1977, Osdene wrote a memorandum entitled "Smoke and Health Defensive Research" in which he characterized the objectives of such research as: (1) anticipating the directions and extent of the pressures relative to smoking and health, (2) assuring the safety of new product components, (3) maintaining experimental capability to test for appropriate biological

effect in any situation, (4) developing the battery of short-term chemical and biological predictors of long-term biological effects and, (5) advising top management on smoking and health strategy and tactics.

When elaborating on the safety of new product components, Osdene said that one part of that would include internal and external biological testing. This document is quite detailed in its recitation of pre-1977 testing both in-house and external. The recitation is of in vivo and in vitro testing.

After a review of the above documents and lengthy discussions with both Drs. Osdene and Wakeham, it seems to me that it is extremely difficult to characterize the biological research program at Philip Morris as other than smoking and health related. The answer to the question "Would such research have been conducted in the absence of a smoking and health controversy?", I think is no. Was such research conducted, in part, as a means of being prepared to take advantage, in a marketing sense, of the results of such research? I think the answer to this question is yes. Was our testing designed to parallel the testing being done by our critics in an attempt to critique their work and to make some determination of its accuracy? Again, I think the answer is yes. Was the research done in the hope that we would see less biological activity in mouse skin painting with various blends? I don't think there is any doubt that the answer is yes. Was the research conducted in order to protect our consumers from more biologically active tobacco blends? Again, I think the answer is yes in the sense that I don't believe we ever went forward with tobacco blends or additives which, when tested, proved to be more biologically active than the blends on the market.

What did we do with the results of our research? What did anyone do with the results of their research other than report them? What did Wynder, the American Cancer Society or anyone else taking positions adverse the company's position do with the results of their research other than report them and eventually rely upon the epidemiological studies?

The research, at least to the extent of the mouse skin paintings, reveals the inherent unreliability of that research. The inhalation studies, both those sponsored by Philip Morris and those sponsored by the critics, show that it is extremely difficult, if not impossible, to develop human type lung cancers in the lungs of animals exposed to whole smoke as a result of inhalation. As of this date, is that not the most important finding from all the biological assays?

Whether the Wakeham/Osdene pleas for in-house biological research were heeded or not (and they were) that research went ahead at FDRL, Hazleton, the American Health Foundation and Inbifo with the results tracking the results in the reported literature.

Philip Morris management was concerned with the marketing advantages that might be realized from the biological research and the advantages to which "good" biological research results could be put in the marketplace (comments of Clifford Goldsmith). In large measure, I believe that top management would have preferred that the results of Philip Morris's biological research not be reported to them unless the results could be used for a marketing advantage. Perhaps they felt some some responsibility for doing this type of research but I don't believe it was of great interest to them or of a high priority. It was certainly preferable to keep the research at some physical distance. Consequently, we see not the purchase of Woodard Laboratories in Washington, D.C., but the purchase of Inbifo in Cologne, Germany. On the other hand, what was there to report? The research being done in the smoking and health area for the period of the late 1950s through late 1970, both by the industry and its critics, was in its early stages and researchers were struggling with the methodology and the manufacture of the equipment in order to be able to conduct this type of research. Let's remember that the major indictment of cigarette smoking was, and still is, based upon epidemiological and not on clinical or biological studies.

My conclusions are: (1) that the company acted responsibly in authorizing the research that was conducted and in monitoring the literature; (2) that the major indictment against cigarette smoking as being a cause of human disease was, in the 1950s, and remains today the epidemiological studies which are inherently flawed; and (3) that the biological research being done by Philip Morris, under contract to Philip Morris, by grantees of CTR and by critics of the industry, still points to the fact that inhalation studies have failed to produce human type lung cancers in the lungs of animals exposed to whole cigarette smoke.